

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

1-24. (Cancelled)

25. (Currently amended) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site; and
- b) a nucleotide sequence to be *trans*-spliced to [[the]] a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

26. (Currently amended) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) a 5' splice site; and
- b) a nucleotide sequence to be *trans*-spliced to [[the]] a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

27. (Currently amended) The cell of Claim 25 wherein the nucleic acid molecule further comprises a 5' ~~donor~~ splice site.

28. (Original) The cell of Claim 25 or 26 wherein the nucleotide sequences to be *trans*-spliced to the target pre-mRNA comprises a nucleotide sequence tag.

29. (Currently amended) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site; and
- b) a nucleotide sequence to be *trans*-spliced to ~~[[the]]~~ a target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

30. (Currently amended) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) a 5' splice site; and
- b) a nucleotide sequence to be *trans*-spliced to ~~[[the]]~~ a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

31. (Currently amended) The cell of Claim 29 wherein the nucleic acid molecule further comprises a 5' ~~donor~~ splice site.

32. (Original) A method of producing a chimeric RNA molecule in a cell comprising: contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site; and
- b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is

trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

33. (Original) A method of producing a chimeric RNA molecule in a cell comprising: contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) a 5' splice site; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

34. (Currently amended) A method of Claim 32 wherein the nucleic acid molecule further comprises a 5' ~~donor~~ splice site.

35. (Original) The method of Claim 32, wherein the chimeric RNA molecule comprises a nucleotide sequence tag.

36. (Currently amended) An eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site; and
- b) a nucleotide sequence to be *trans*-spliced to ~~[[the]]~~ a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

37. (Currently amended) An eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) a 5' splice site; and
- d) a nucleotide sequence to be *trans*-spliced to [[the]] a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

38. (Currently amended) The vector of Claim 36 wherein the nucleic acid molecule further comprises a 5' ~~donor~~ splice site.

39. (Currently amended) An expression library comprising recombinant expression vectors wherein said vectors expresses a nucleic acid molecule comprising:

- a) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site; and
- d) a nucleotide sequence to be *trans*-spliced to [[the]] a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

40. (Currently amended) An expression library comprising recombinant expression vectors wherein said wherein said vector expresses a nucleic acid molecule comprising:

- a) a 5' splice site; and
- b) a nucleotide sequence to be *trans*-spliced to [[the]] a target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

41. (Currently amended) The expression library of Claim 39 wherein the nucleic acid molecule further comprises a 5' ~~donor~~ splice site.

42. (Original) The expression library of Claim 39 or 40 wherein the nucleotide sequence to be spliced to the target pre-mRNA comprises a nucleotide sequence tag.

43. (Original) A method for mapping exon-intron boundaries in pre-mRNA molecules comprising:

- (i) contacting a nucleic acid molecule to a target pre-mRNA molecule, under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric mRNA;
- (ii) amplifying the chimeric mRNA molecule;
- (iii) selectively purifying the amplified molecule; and
- (iv) determining the nucleotide sequence of the amplified molecule thereby identifying the intron-exon boundaries.

44 - 91. (Cancelled)

92. (New) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein said target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

93. (New) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein said target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

94. (New) The cell of Claim 92, wherein the target binding domain is between 15-500 nucleotides.

95. (New) The cell of Claim 92, wherein the target binding domain is between 15-411 nucleotides.

96. (New) The cell of Claim 92, wherein the target binding domain is between 200-411 nucleotides.

97. (New) The cell of Claim 93, wherein the target binding domain is between 15-500 nucleotides.

98. (New) The cell of Claim 93, wherein the target binding domain is between 15-411 nucleotides.

99. (New) The cell of Claim 93, wherein the target binding domain is between 200-411 nucleotides.

100. (New) The cell of Claim 92 wherein the nucleic acid molecule further comprises a 5' splice site.

101. (New) The cell of Claim 92 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice site.

102. (New) The cell of Claim 93 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 5' splice site.

103. (New) The cell of Claim 92 wherein the nucleic acid molecule further comprises sequences encoding a translatable protein product.

104. (New) The cell of Claim 92 or 100 wherein the nucleic acid molecule further comprises a nucleotide sequence containing a translational stop codon.

105. (New) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and the target

binding domain binds to a target pre-mRNA expressed within a cell;

- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

106. (New) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

107. (New) The cell of Claim 105, wherein the target binding domain is between 15-500 nucleotides.

108. (New) The cell of Claim 105, wherein the target binding domain is between 15-411 nucleotides.

109. (New) The cell of Claim 105, wherein the target binding domain is between 200-411 nucleotides.

110. (New) The cell of Claim 106, wherein the target binding domain is between 15-500 nucleotides.

111. (New) The cell of Claim 106, wherein the target binding domain is between 15-411 nucleotides.

112. (New) The cell of Claim 106, wherein the target binding domain is between 200-411 nucleotides.

113. (New) The cell of Claim 105 wherein the nucleic acid molecule further comprises a 5' splice site.

114. (New) A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

115. (New) A method of producing a chimeric RNA molecule in a cell comprising:
contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

116. (New) The method of Claim 114, wherein the target binding domain is between 15-500 nucleotides.

117. (New) The method of Claim 114, wherein the target binding domain is between 15-411 nucleotides.

118. (New) The method of Claim 114, wherein the target binding domain is between 200-411 nucleotides.

119. (New) The method of Claim 115, wherein the target binding domain is between 15-500 nucleotides.

120. (New) The method of Claim 115, wherein the target binding domain is between 15-411 nucleotides.

121. (New) The method of Claim 115, wherein the target binding domain is between 200-411 nucleotides.

122. (New) The method of Claim 114 wherein the nucleic acid molecule further comprises a 5' splice site.

123. (New) The method of Claim 114 wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

124. (New) The method of Claim 114 wherein the chimeric RNA molecule comprises sequences encoding a toxin.

125. (New) A nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

126. (New) A nucleic acid molecule comprising :

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and
- e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

127. (New) The nucleic acid molecule of Claim 125, wherein the target binding domain is between 15-500 nucleotides.

128. (New) The nucleic acid molecule of Claim 125, wherein the target binding domain is between 15-411 nucleotides.

129. (New) The nucleic acid molecule of Claim 125, wherein the target binding domain is between 200-411 nucleotides.

130. (New) The nucleic acid molecule of Claim 126, wherein the target binding domain is between 15-500 nucleotides.

131. (New) The nucleic acid molecule of Claim 126, wherein the target binding domain is between 15-411 nucleotides.

132. (New) The nucleic acid molecule of Claim 126, wherein the target binding domain is between 200-411 nucleotides.

133. (New) The nucleic acid molecule of Claim 125 wherein the nucleic acid molecule further comprises a 5' splice site.

134. (New) The nucleic acid molecule of Claim 125 or 126 wherein the nucleic acid molecule further comprises sequences encoding a translatable protein product.

135. (New) The nucleic acid molecule of Claim 134 wherein the translatable protein product is a toxin.

136. (New) An expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;

- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

137. (New) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

138. (New) The eukaryotic expression vector of Claim 136, wherein the target binding domain is between 15-500 nucleotides.

139. (New) The eukaryotic expression vector of Claim 136, wherein the target binding domain is between 15-411 nucleotides.

140. (New) The eukaryotic expression vector of Claim 136, wherein the target binding domain is between 200-411 nucleotides.

141. (New) The eukaryotic expression vector of Claim 137, wherein the target binding domain is between 15-500 nucleotides.

142. (New) The eukaryotic expression vector of Claim 137, wherein the target binding domain is between 15-411 nucleotides.

143. (New) The eukaryotic expression vector of Claim 137, wherein the target binding domain is between 200-411 nucleotides.

144. (New) The vector of Claim 136 wherein the nucleic acid molecule further comprises a 5' splice site.

145. (New) The expression vector of Claim 136 or 137 further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the splice site.

146. (New) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein said target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and

- d) nucleotide sequence to be *trans*-spliced to the target pre-mRNA;
wherein said nucleic acid molecule is recognized by nuclear
splicing components within the cell.

147. (New) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein said target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

148. (New) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

149. (New) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

150. (New) A method of producing a chimeric RNA molecule in a cell comprising:
contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred

nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;

- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

151. (New) A method of producing a chimeric RNA molecule in a cell

comprising:

contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

152. (New) A nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

153. (New) A nucleic acid molecule comprising :

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;

- c) a spacer region that separates the 5' splice site from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and
- e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

154. (New) An expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

155. (New) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains wherein said target binding domain is at least 15-30 nucleotides and up to several hundred nucleotides in length and wherein the target binding domain binds to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.